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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,854	03/07/2002	Felix Kratz	25048/20	6344

7590 11/13/2006

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 11/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,854	KRATZ, FELIX	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,20-30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) *21 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,20,22-24,26-30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicant's election of the species in the reply filed on November 13, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 21 and 25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 13, 2003.

2. The Sequence Listing filed February 6, 2006 is approved.

3. The disclosure is objected to because of the following informalities: SEQ ID NOS need to be inserted after all amino acid sequences subject to the sequence disclosure rules. See 37 CFR 1.821(d). Such sequences are present at pages 23, 24, and 35-37 of the specification, and in Figure 2B. For sequences present in the drawings, the SEQ ID NOS are preferably inserted into the Brief Description of the Drawings. Applicants are requested to re-supply by appropriate amendment the top line of page 25 of the specification. The current scanned image is partially obscured due to hole punching in the original source. Appropriate correction is required.

The amendments to the specification filed October 23, 2006 have not been entered because they are not in proper format under 37 CFR 1.121(b)(1)(ii). The changes to the specification have not been marked with underlining and strike-through as required by the rule. The examiner can not identify any change which has been made to paragraph [0052]. Paragraph [0054] of the amendment does not correspond to paragraph [0054] of the specification, but rather seems to combine at least parts of paragraphs [0052] and [0054] of the specification while skipping paragraph [0053] of the specification. The amendment to paragraph [0054] also inserts

"SEQ ID NO:6" after two dipeptide sequences which are not subject to the sequence disclosure rules and which do not correspond to SEQ ID NO:6 as defined in the Sequence Listing filed February 6, 2006. The SEQ ID NOS inserted into paragraph [0055] do not correspond to the amino acid sequences occurring in the paragraph. The amendment to paragraph [0055] did not insert a SEQ ID NO after the amino acid sequence occurring in the second-to-last line of the paragraph. The amendment did not propose inserting a SEQ ID NO after the amino acid sequences recited in page 35 or at page 37, lines 3 and 5-6. With respect to the amino acid sequence occurring in Figure 2B, all amino acid sequences having four or more specifically defined residues are subject to the sequence disclosure rules. The rules apply whether the sequences are claimed or not. See, e.g., MPEP 2421.02, second paragraph, and 2422.02, second paragraph. That the sequence in question might be a digest is irrelevant to the applicability of the rules. With respect to the top line of page 25 of the specification, Applicants are requested to re-supply only the paragraph containing the line in question and not subsequent paragraph [0058].

4. Claims 18, 20, 22-24, 26-30, and 32-34 are objected to because of the following informalities: At claim 18, lines 5 and 14, "cysteine" is misspelled. Appropriate correction is required.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 18, 20, 22-24, 26, 27, and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 98/10794. (The examiner will rely upon U.S. Patent No. 6,310,039 as a translation of the WO Patent Application '794. All citations in this rejection are to the U.S. patent.) The WO Patent Application '794 teaches a carrier drug conjugate in which doxorubicin is linked via a hydrazone linkage through phenylacetic acid to a maleimide group, which is conjugated to thiolated albumin. Seven molecules of doxorubicin are linked per molecule of albumin. See, e.g., column 22, lines 33-42. Hydrazone linkages are hydrolyzable in acidic mediums. Because there is one reducible cysteine group per molecule of albumin, the ratio of doxorubicin bound per mole of reducible cysteine group in the conjugates of the WO Patent Application '794 is 7. Note that while claim 18 requires the carrier to comprise at least one reducible cysteine group, it does not actually require the cysteine group to be in reduced form; and that while the claim recites a ratio of bound drug per reducible cysteine group, it does not actually require that the drug be bound to the cysteine group. With respect to instant claims 33 and 34, the conjugate of the WO Patent Application '794 is deemed to anticipate the instant kit claims, whose only recited element is the carrier-drug conjugate.

7. Claims 33 and 34 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/10794. Application of the WO Patent Application '794 is the same as in the above rejection of claims 18, 20, 22-24, 26, 27, and 32-34. To the extent that the WO Patent Application '794 might not teach its conjugate in kit form, it would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to package the conjugate of

the WO Patent Application '794 in kit form because kits are routinely used in the pharmaceutical arts for purposes of storage, transportation, measurement, and administration.

8. Claims 18, 20, 22-24, 26-30, and 32-34 are rejected under 35 U.S.C. 102(a) as being anticipated by the Kratz et al article (J. Med. Chem., Vol. 43, pages 1253-1256). The Kratz et al article teaches treating albumin with dithiothreitol so that approximately one mole sulfhydryl group (from Cys34) per molecule of albumin is obtained. The treated albumin is then reacted with the doxorubicin derivative of Figure 1. The doxorubicin derivative of the Kratz et al article has the same structure as Applicants' elected species. The pure conjugate has a drug:albumin ratio of approximately 0.9:1. See, e.g., page 1254, column 1, second full paragraph. With respect to instant claim 32, while the Kratz et al article does not intend to administer the pure conjugate in vivo to animals with cancer (instead, the Kratz et al article intends to administer the doxorubicin derivative of Figure 1 in vivo, where it reacts with endogenous albumin), an intended use limitation does not impart patentability to product claims where the product is otherwise anticipated by the prior art. With respect to instant claims 33 and 34, the pure conjugate of the Kratz et al article is deemed to anticipate the instant kit claims, whose only recited element is the carrier-drug conjugate.

9. Claims 33 and 34 are rejected under 35 U.S.C. 103(a) as being obvious over the Kratz et al article (J. Med. Chem., Vol. 43, pages 1253-1256). Application of the Kratz et al article is the same as in the above rejection of claims 18, 20, 22-24, 26-30, and 32-34. To the extent that the Kratz et al article might not teach its conjugate in kit form, it would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to package the conjugate of

the Kratz et al article in kit form because kits are routinely used in the pharmaceutical and chemical assay arts for purposes of storage, transportation, measurement, and administration.

10. Applicant's arguments filed October 23, 2006 have been fully considered but they are not persuasive.

The rejections over the Firestone et al article (Journal of Controlled Release, Vol. 39, pages 251-259) are withdrawn in view of the amendments to the claims requiring that the carrier be albumin.

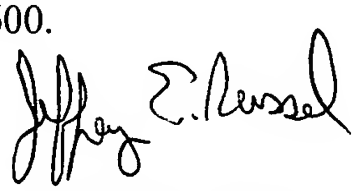
The rejections based upon the WO Patent Application 98/10794 are maintained. At several places in Applicant's remarks, Applicant contends that his drug moiety is bound to the cysteine group of the carrier. The examiner does not agree. There is no claim language which requires the drug moiety to be bound to the cysteine group of the carrier. For example, claim 18, lines 14-15, includes the phrase "per mole of reducible cystein group", but this phrase helps define a molar ratio and does not indicate that that anything is bound to the cystein. Claim 18, lines 14-15, also includes the phrase "at least 0.7 mol of drug is bound... through said thiol binding group", but does not state to what the thiol binding group is bound. While the examiner agrees that there are examples in Applicant's specification in which the drug is bound to the cysteine group of the carrier, limitations found only in the specification will not be read into the claims. Patentability must be based upon claimed, not unclaimed, differences over the prior art.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel
November 7, 2006